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# Heterogeneous Catalytic Transfer Hydrogenation and Its Relation to Other Methods for Reduction of Organic Compounds

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## I. Introduction

Reduction of organic compounds is important synthetically both in the laboratory and in industry. There are many methods of effecting reduction which may or may not lead to hydrogenation, but in this review only processes leading to the addition of hydrogen or replacement of a functional group by hydrogen will be considered. Further, this review will be concerned mostly with those processes that can be effected by heterogeneous catalysis using molecules other than molecular hydrogen as the source of hydrogen. Reduction of organic functional groups can be categorized into (i) addition of hydrogen to unsaturated groups as, for example, in the reduction of ketones to alcohols and (ii) addition of hydrogen across single bonds leading to cleavage of functional groups (hydrogenolysis). Removal of oxygen as a reductive process, as in the deoxygenation of oxiranes to alkenes, will not be discussed.

Of all the methods available for addition of hydrogen to organic compounds, heterogeneous catalytic transfer reactions have been relatively underutilized. This lack of popularity can be traced to the relatively meager success of much of the earlier research which suggested that the technique was of only limited scope and could provide only modest yields of products. The early pioneering work by Braude[1] was largely ignored because of poor yields and long reaction times, but the situation has changed considerably following the appearance[4] of a stimulating review and the introduction of greater catalyst loadings and different hydrogen donors.[2] Another reason for the underutilization of transfer reduction has been the very successful exploitation of molecular hydrogen and hydrides for reduction of organic compounds.

In comparison with catalytic reduction using molecular hydrogen, transfer reduction using hydrogen donors has real and potential advantages. Molecular hydrogen, a gas of low molecular weight and therefore high diffusibility, is easily ignited and presents considerable hazards, particularly on the large scale; the use of hydrogen donors obviates these difficulties in that no gas

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SCHEME XIV

$$R_2CHOH \longrightarrow R_2CO + H_2 \quad (a)$$

$$2R_2CHOH \longrightarrow R_2CHOCHR_2 + H_2O \quad (b)$$

$$3R_2CHOH \longrightarrow (R_2CH_2)_2 + R_2CO + 2H_2O \quad (c)$$

$$2R_2CHOH \longrightarrow R_2CH_2 + R_2CO + H_2O \quad (d)$$

$$\left.\begin{matrix} R_2CHOH \\ + \\ R'_2CHOH \end{matrix}\right\} \longrightarrow R_2CH_2 + R'_2CO + H_2O \quad (e)$$

## B. Hydrogen Donors

### 1. Homogeneous Catalysis

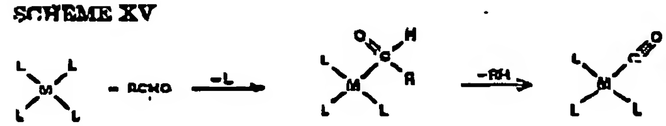
Although homo- and heterogeneous catalysts can utilize common types of compounds as hydrogen donors, it is more often the case that different types of compounds are favored in the two systems. The more active hydrogen donors for homogeneous catalysis appear to be principally alcohols, hydroaromatics, cyclic ethers, and occasionally formic and ascorbic acids whereas, for heterogeneous catalysis, the more widely used donors tend to be hydrazine, formic acid and formates, phosphinic acid and phosphinates, indoline, and cyclohexene. There is no clear division between the two types, but some of the hydrogen donors which are active for heterogeneous catalysts are water-soluble inorganic salts and cannot be used with many homogeneous catalysts. More recently, trialkylsilanes and trialkylstannanes have proved to be good hydrogen donors in both homo- and heterogeneous catalysis.[40] Whereas tri-*n*-butylstannane reduced $\alpha,\beta$-unsaturated aldehydes in methanol under fairly drastic conditions,[203] in the presence of $Pd(PPh_3)_4$ and a promotor, the reduction can be achieved in 10 min at room temperature.[40]

Of the alcohols, secondary ones have proved to be the best hydrogen donors and it is the hydrogen on the carbon attached to the hydroxyl ($\alpha$-hydrogen) which is transferred in the first reductive step. Tertiary alcohols having no $\alpha$-hydrogen atoms are not hydrogen donors and under the influence of catalysts, tend to condense to form ethers or to eliminate water to form alkenes.[71] Primary alcohols may or may not be good hydrogen donors and form a special case which is discussed more fully below.

Secondary alcohols in the presence of a homogeneous catalyst, but in the absence of a hydrogen acceptor may react in one of five principal modes viz., by dehydrogenation, dehydration, reductive coupling, disproportionation, and hydrogenolysis (equations a–d, respectively); where a second type of alcohol is involved, a reaction (e) similar to (d) may occur.[103,127] In the presence of a suitable hydrogen acceptor, reaction (a) usually occurs with the hydrogen being transferred to the acceptor, but not of course as the molecular hydrogen of reaction (a), and the secondary alcohol is transformed into a ketone.

An $\alpha$-hydrogen of a primary alcohol is less likely than that of a secondary alcohol to react as a hydride species, because of the smaller electron-releasing inductive effect of one alkyl group as against two. Nevertheless, ethanol and 1-propanol have been used successfully for the transfer reduction of carboboranes,[204] aldehydes,[110] alkynes,[117] dienes,[121] and alkenes.[118] Benzyl alcohol is active in the reduction of double bonds in unsaturated ketones,[71,84] acids and esters,[77,95] and cycloalkenes,[115] and in the reduction of aldehydes to alcohols.[75,110] Even so, primary alcohols may not be rewarding as hydrogen donors because aldehydes, the products of their dehydrogenation, act as catalyst poisons. Also, aldehydes when complexed to some homogeneous catalyst systems are decarbonylated so that CO becomes a ligand which may inactivate the catalyst (Scheme XV).[67,118,121,205] In some catalyst systems in which ethanol or benzyl alcohol have been used successfully as hydrogen donors, attempts to detect such carbonyl complexes were unsuccessful.[115] There are reports of the resistance of aldehydes to decarbonylation[110] and, in contrast, others in which the aldehydes are decarbonylated to give a new active catalyst as a result of incorporation of the CO as a ligand.[200]

SCHEME XV




Diols, some primary and some secondary, have been used as hydrogen donors even though they yielded aldehydes by dehydrogenation. Ethane-1,2-diol, cyclohexane-1,2-diol, hexane-1,6-diol, and butane-2,3-diol have been utilized in the catalytic transfer reduction of alkenes to alkanes[100,105,106,110,140] and of ketones to alcohols.[207] Similarly, polyols such as furanoses, pyranoses, and poly(vinyl alcohol) have been employed to reduce unsaturated ketones to saturated ketones,[76,78,81,97,187,208,209] and $\alpha,\beta$-unsaturated acids to saturated acids.[85] In the absence of a hydrogen-acceptor substrate, sugars undergo mutual oxidation/reduction to give, in place of two aldehyde groups, an alcohol and a lactone.[97,209] The best hydrogen donors among the sugars have been found to be glucoses or glucosides having an arrangement of three *cis*-hydroxyl groups which provide the best coordination to the catalytic metal.[78,182,208]

Despite the use of a variety of alcohols, 2-propanol remains the most popular donor, because of its simplicity, cheapness, availability, and the ease of removal of both it and its dehydrogenation product, acetone, from reaction systems. The mechanism of hydrogen transfer from 2-propanol to a ketone substrate using the catalyst, $RhCl(PPh_3)_3$, has been very extensively investigated so that most details of the mechanism are clear.[210] A synergist for this reaction is potassium hydroxide which is believed to be effective by removing a proton from the reacting complex during part of the catalytic cycle. Certainly, many other homogeneous catalyst systems using an alcohol as the hydrogen donor appear to need base (KOH) for their activity.[74,88,99,211–218] Scheme XVI indicates how this synergistic activity may arise by promoting the transfer of a hydride ion from an alkoxy radical onto an adjoining coordinated ketone. Despite this careful work, the full mechanistic details of general catalytic transfer reduction are not understood completely. Kinetic studies to compare the transfer reduction of cycloalkenes and aldehydes with $RuH_2(PPh_3)_4$ as catalyst and 2-propanol as hydrogen

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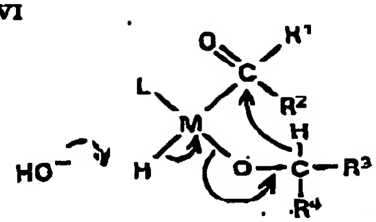
SCHEME XVI




donor revealed a large kinetic isotope effect in the reduction of alkenes[113] (transfer of hydrogen being the rate-limiting step) and no isotope effect with aldehydes.[110] This result does not invalidate the overall view of this type of hydrogen transfer, since it probably reflects only the different timing of certain steps of the whole reaction of cycloalkenes as compared with aldehydes.

Of other kinds of hydrogen-donor that have been used, some mention should be made of cyclic ethers like dioxane[69,82] and dihydrofuran[110] and of aldehydes[120] and formic acid.[104,116,120] Hydroaromatic compounds, which may be concomitantly dehydrogenated to aromatic compounds, have been used widely as hydrogen donors. For example, most functional groups can be reduced by using tetrahydroquinoline, piperidine, pyrrolidine, and indoline (ref 72, 105, 107, 109, 114, 128, 140, 141) and the hydrocarbons, indan and tetralin have served to reduce aldehydes to alcohols (ref 75, 110, 142). Aromatization is not necessarily the driving force of these reactions because, although indoline is dehydrogenated to indole in these reactions,[140,141] piperidine does not yield pyridine.[141] The effects of these hydrogen donors are not uniform so that successful use of one donor in one situation does not imply its success in another. Aldehydes can be reduced to alcohols in high yields using $RuH_2(PPh_3)_4$ at 140 °C with 2,5-dihydrofuran or 2-propanol as hydrogen-donor,[110] but the same donors with $RhCl_3$ at 120 °C were ineffective in reducing nitrobenzene to aniline.[72]

Some leading references to the use of the above hydrogen donors in catalytic transfer reduction are given in Table III.

### 2. Heterogeneous Catalysis

Some of the best hydrogen donors for heterogeneous catalytic transfer hydrogenation comprise of simple molecules such as cyclohexene, 1,4-cyclohexadiene, hydrazine, formic acid and formates, phosphinic acid and phosphinates, phosphorous acid and phosphites, and sodium tetrahydroborate (see Table IV). Generally, these donors are used with noble-metal catalysts (either finely divided or supported on carriers), but, sometimes with other metals such as copper and nickel, often for use at higher temperatures. With the noble metals, particularly Pd, Pt, and Rh these hydrogen donors give up hydrogen to the substrate under mild conditions with reaction temperatures rarely exceeding 100 °C. After giving up their hydrogen, the other reaction products from the hydrogen donors are frequently easily removable from the reaction system. Thus, formic acid exhibits two modes of decomposition[214] and may give $CO_2$ or CO as its non-hydrogen containing side products, depending on the catalyst used. Similarly, hydrazine decomposes to give either

TABLE III. References to Hydrogen Donors Used in Homogeneous Catalytic Transfer Hydrogenation.

| hydrogen donor | ref |
|---|---|
| cyclohexene | 72, 75, 109 |
| indan | 142 |
| tetralin | 75, 110, 290 |
| indoline | 72, 104, 105, 107, 109, 114, 140, 141 |
| tetrahydroquinoline | 107, 114, 140, 141 |
| dihydrofuran | 75, 110 |
| dioxan | 69, 82 |
| ethanol | 115, 117, 121, 204 |
| propan-2-ol | 67, 73, 74, 75, 98, 99, 105, 110, 113, 115, 122, 205, 210–213, 290–293 |
| pentan-2-ol | 118, 294 |
| 2-methoxyethanol | 295 |
| benzyl alcohol | 71, 75, 84, 95, 115 |
| tetrahydrofurfurol | 295 |
| steroids | 102 |
| 1,2-ethanediol | 118, 207 |
| 2,3-butanediol | 106, 140 |
| 1,2-cyclohexanediol | 105, 106, 140 |
| polyvinyl alcohol | 79 |
| ascorbic acid | 210 |
| sugars | 76, 78, 81, 90, 97, 105, 106, 208, 209 |
| phenols | 119 |
| formic acid | 296, 297 |

TABLE IV. References to the Commoner Hydrogen Donors Used in Heterogeneous Catalytic Transfer Hydrogenation

| hydrogen donor | ref |
|---|---|
| cyclohexene | 47, 70, 167, 170, 173, 181, 184, 185, 186, 189, 226, 285, 288 |
| cyclohexadiene | 126, 281 |
| limonene | 70, 154 |
| ethanol | 177 |
| propan-2-ol | 137, 175, 177 |
| benzyl alcohol | 166 |
| benzhydrol | 127 |
| hydroquinone | 289 |
| sugars | 182 |
| indoline | 47, 70 |
| N-benzylaniline | 178 |
| formic acid | 47, 70, 128, 214, 281 |
| formates | 128, 129, 180, 225 |
| phosphinic acid | 128, 184 |
| sodium phosphinate | 128, 145, 170, 192 |
| sodium tetrahydroborate | 47 |
| hydrazine | 152, 171, 174, 192 |

nitrogen or ammonia together with hydrogen, but phosphinic acid (hypophosphorous acid) is normally oxidized to phosphorous acid by water in giving up its hydrogen, rather than undergoing decomposition. The mode of reaction of formic acid or hydrazine depends markedly on conditions of temperature, pressure, and type of catalyst. For example, in the gas phase over a copper catalyst, formic acid decomposes through the formate anion whereas, with nickel, it decomposes via an anhydride.[214,215] The different modes of decomposition of hydrazine are revealed by the types of functional groups that can be reduced with this hydrogen donor.[216] The decomposition of hydrazine over metals such as Pd tends to yield mostly hydrogen and nitrogen and can lead to hydrogenolysis of C–O bonds[174,192] or reduction of nitro groups[152,171] whereas its decomposition with oxidizing agents tends to produce diimide initially. The decomposition of hydrazine via diimide is characterized by the fact that diimide adds hydrogen to symmetrical (nonpolar) double bonds like those found in alkynes and alkenes, but not polar bonds like carbonyl.[216] The mode of decomposition of tetrahydroborates with catalysts is obscure. Although nitro compounds are not reduced directly by sodium tetra-

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